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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,923	12/21/2001	Brian Gaither Bates	AM100369	9899

25291 7590 02/10/2004

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EXAMINER	
TURNER, SHARON L	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,923	BATES ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4-9-02*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 1-19 and 36 in the Paper of 11-13-03 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

3. Claims 1-19 and 36 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial, credible asserted utility or a well established utility.

The specification discloses at pp. 1-5, that the invention is related to nucleic acids and peptides referred to as metabotropic glutamate receptor subtype modulatory proteins (also referred to herein as the mGluR5M proteins or the mGluR5M family. The peptides are noted to be related by homology to mGluR5 receptor proteins, particularly in N- and C-terminal regions, hence the name. In addition, the molecules, mimics and/or modulators are noted to be useful in regulating a variety of cellular processes. For example the specification notes uses related to screening assays, detection assays, chromosomal mapping, tissue typing, prevention, forensics, diagnostics, prognostics, monitoring in clinical trials, prophylaxis, therapeutics and pharmacogenomics, see in

particular pp. 50-65. In particular, pp. 10 of the specification notes that, "a "mGluR5M activity", "biological activity of mGluR5M" or "functional activity of mGluR5M" includes modulation (e.g., enhancement or inhibition) of glutamate receptor functions and/or activities, in particular, metabotropic glutamate receptor functions and/or activities (e.g., mGluR5 functions and/or activities)... In a preferred embodiment, a mGluR5M activity is at least one of the following activities: (1) modulation of G protein linked second messenger signaling pathways (e.g., modulation of diacylglycerol and/or inisitol triphosphate-mediated signaling pathways), for example, signaling pathways involved in neuronal cell signalling and nervous system function; (2) modulation of glutamatergic transmission; (3) modulation of neuronal excitability; (4) regulation of synaptic transmission; (5) modulation of neurotransmitter release (e.g., glutamate release); (6) regulation of voltage-dependent and/or voltage-independent and/or ligand-gated ion channels (e.g. , K+ channels or Ca2+ channels); (7) regulation of neuronal development (e.g., regulation of neuronal differentiation, migration and/or survival in the developing brain); (8) modulatoin of nervous system function; and (9) modulation of neurodegenerative processes (e.g., acute or chronic neurodegenerative processes). In yet another embodiment, a mG1uR5M 5 activity is modulation of mG1uR5 dimerization e.g., mG1uR5a and/or mGluR5b dimerization) and/or dimerization of other mGluR family members (e.g., mGluR1 dimerization)." In addition, the functions noted are said to be useful for example in, "treating, for example, neurodegenerative disorders and/or diseases (e.g., motor neuron disease (MND), amyotrophic lateral sclerosis (ALS), Huntington's chorea, Parkinson's disease and Alzheimer's disease), stoke, the brain

damage occurring acutely after status epilepticus, cerebral ischemia or 'tratzmatic brain injury and/or movement disorders.

Yet the specification provides no specific and detailed information as to the noted laundry list of possible activities, functions and uses for the specific mGluR5M identified molecules of SEQ ID NO's:1-3. The specification fails to exemplify any specific and substantial use of the claimed nucleic acids and/or protein encoded thereby. In particular, the significance of the molecule, its functions, effects and substantial utility are lacking. While the specification contemplates the various reagents as useful in the noted molecular techniques of experimentation, such utilities are not specific or substantial because the uses merely rely on the inherent properties of any nucleic acid to hybridize (bind) and/or encode and any peptide to bind and/or stimulate an immune response. The uses stem from the broad generic class of properties applicable to any nucleic acid or peptide molecule. Thus, the disclosed nucleic acids and peptides merely constitute research reagents for further experimentation to discover their "real-world" use. The contemplated uses also do not constitute well-established utilities because their functional significance has yet to be established. The peptides are merely disclosed as being related to glutamate receptor proteins and neuronal cell function and/or cell signaling in general. Yet there is no known sequence structure or function disclosed or recognized as being related to any of a multitude of neurological or neuron associated functions. In addition, the specification does not teach any conserved nucleic or amino acid positions critical to a particular neuron activity, function or phenotype. The biological significance remains to be established such that the artisan

can use the peptides and/or nucleic acids to provide public benefit. No "real world" utility is disclosed.

As recognized by Skolnick et al., Trends in Biotech., 18(1):34-39, 2000, the skilled artisan is well aware that there is an unpredictable nature in the ability of encoding nucleic acids to predict structural and functional activities for any particular protein or protein family, and that even when highly homologous and conserved residues are known only experimental research can confirm the artisan's best guess, see in particular Skolnick, abstract and Box 2. Moreover, Schoepp et al., notes different function even amongst metabotropic glutamate receptors in relation to brain function and pathology, see in particular TIPS, 14(1):13-20, Jan. 1993. Thus, the assignment of instant SEQ ID NO's: 1-3 as mGluR5M molecules and the brief mention of its' relationship to glutamate receptors in general, fails to define a specific or substantial asserted utility or well-established utility for the claimed sequences.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-19 and 36 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial, credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

6. Claims 1-19 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing

to comply with the enablement requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Applicants claims are directed to peptides with greater than single amino acid substitutions as encompassed by % identity, to "N-terminal mGluR-like domains" and to "C-terminal unique domains."

The specification does not enable the broad scope of the claims which encompasses a multitude of analogs or equivalents because the specification does not teach which residues can or should be modified such that requisite functionality is maintained, note utility rejection above. The specification provides essentially no guidance as to which of the essentially infinite possible choices is likely to be successful in any particular use and the skilled artisan would not expect functional conservation amongst homologous sequences. Thus, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims.

As to the % identity "N-terminal mGluR-like domain" and "C-terminal unique

domain" variants, the skilled artisan recognizes that nucleic and amino acid alterations may lead to differences in function. For example, the skilled artisan recognizes as noted in Skolnick et al., above and as further exemplified by Choh, PNAS 77(6):3211-14, 1990, that one or more amino acid deletions, insertions or substitutions including truncations results in unpredictable effects in the resulting biological molecule, its' biological function, the ability to bind and/or exhibit similar immunoreactivity. The specification teaches no structural or functional activities of the noted variants and fails to teach any residues which may be exchanged while retaining requsite activity or function. In particular, ther is no significance or function for the variant molecules. As to the nucleic acids, the skilled artisan recognizes that encoding nucleic acids are dependent upon the structural nucleotides and their relationship to the genetic code and translational signals. The specification fails to note those nucleic acid molecules that capable of encoding the requisite peptides. As noted above the peptide structures and their pertinent sequences are insufficiently disclosed and/or enabled to the full scope of the claim.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed sequences without further undue experimentation.

7. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of ATCC Accession Number PTS-2775. Because it is not clear that cell lines possessing the properties of ATCC Accession Number PTS-2775 are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of ATCC Accession Number PTS-2775, a suitable deposit for patent purposes is required. Accordingly, filing of evidence of the reproducible production of the cell line claimed in claim 12, is required. Without publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell line is an unpredictable event.

There is insufficient assurance that all required deposits have been made and all the conditions of 37 CFR § 1.801-1.809 have been met.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of the patent on this application. These requirements are necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR § 1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a

period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that ATCC Accession Number PTS-2775 described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR § 1.801-1.809 for further information concerning deposit practice.

8. Claims 1-11, 15-19 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application

was filed, had possession of the claimed invention. This is a written description rejection.

The specification describes SEQ ID NO:1-3 representing mGluR5M nucleic and polypeptide sequences yet no functional significance or activity is described for the disclosed sequences. The claims encompass polypeptides comprising fragments and homologues, i.e., polypeptides that vary substantially in length and amino acid composition. In particular, the language of the claims is directed to % identity, hybridizing sequences under stringent conditions, N-terminal mGluR-like domains and C-terminal unique domains.

The instant disclosure of a single polypeptide, that of SEQ ID NO's:1-3 with no instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in Regents of the University of California v Eli Lilly & Co, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polypeptide sequence, that of SEQ ID NO: 2 and no other amino acid sequences that are proposed to possess the same activity. The specification similarly fails to describe either the structural or functional characteristics of the N- and C-terminal domains.

Given the unpredictability of homology comparisons as noted above, see in particular Skolnick et al., and Choh et al., and the fact that the specification fails to provide objective evidence that any other additional sequences are indeed species of the claimed genus it cannot be established that a representative number of species have been disclosed to support the genus claim. No activity is set forth for the additional sequences. The specification further sets forth a proposed consensus sequence for the genus (% identity), yet there is no correlation or nexus provided between possession of such structural featurea and any encompassed function of SEQ ID NO's:1-3 such that it is clearly conveyed that possession of any polypeptide having this structural region, any part thereof or percent similarity in common would possess

any defined activity or function and the stringent hybridization conditions are not specified. Thus, the claim recitations lack adequate written description support.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

10. Claims 1-11, 14-19 and 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Wong et al., US Patent Application Publication US 2002/0142952, filed 3-29-01 and published 10-3-02.

Wong et al., teach polynucleotides encoding novel secreted proteins, nucleic acids, vectors and mammalian host cells for expression of the recombinant polypeptide, see in particular Abstract, pp7-8 and claims. In particular Wong et al., teach sequence 61 which shares 99.73 % identity to instant SEQ ID NO:2 differing only in residue 1 of SEQ ID NO:2 which is the N-terminal Methionine. The nucleic acid of instant SEQ ID NO:3 shares 99.8% identity with Wong SEQ ID NO:61 differing only at residues 1-2 of the sequence which are absent and instant SEQ ID NO:1 shares 97.9% identity with Wong SEQ ID NO:61 in that the sequence discloses both N- and C-terminal up- and

down-stream sequences that are non-encoding. Thus, the reference teachings anticipate the claimed invention.

Status of Claims

11. No claims are allowed.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
February 5, 2004